

EXHIBIT 4

Fish and Wildlife Service
Preparatory Notes for 12/3/03 Meeting
Use of Surrogate Species

The Fish and Wildlife Service has expressed concern that tests by EPA's Office of Pesticide Programs in support of pesticide registration address only a limited number of species, and most specifically do not include tests on certain classes of species. Recognizing the EPA is not capable of immediately generating new data for these classes of species, the question becomes what data is available, and how best to use available data – including existing tests on surrogate species – to evaluate risk to listed species of these classes. The species classes of primary concern to the FWS are amphibians, freshwater mussels, and reptiles. We understand NOAA Fisheries may have similar concerns about marine mammals.

From the FWS's perspective, the first priority to address this issue should be a process to ensure that any available tests on these species classes would be obtained during EPA's evaluation process. In other words, existing test data on the effect of a certain pesticide on amphibians would normally be preferable to tests using a surrogate species in place of amphibians, and EPA's process should establish a reliable expectation that the test would be found and evaluated. Evaluation of such a test would include review of the extent to which the results are reliable. If tests exist on pesticides that are chemically similar to the pesticide in question, the test may be evaluated to explain to what extent the test data may be used. That is, EPA would evaluate the uncertainty of using a non-amphibian as a surrogate to the uncertainty of using an amphibian-based test on a different, but similar, pesticide.

By focusing on this point as its primary concern, the FWS intends to assert that test data frequently may be available about a species in a class not represented by the existing suite of surrogates, even if that data would not be sufficient to fully demonstrate the extent to which the sensitivity of that class may or may not be represented by the sensitivity of a species from another class.

Presuming that, in many instances, no specific data will exist concerning the effect of the pesticide in question on these classes of species, tests using surrogate species will likely constitute the best available information. Both the Services and EPA recognize that there can be great variability in the sensitivity of species to any given pesticide. EPA's overview of OPP's risk assessment process indicated that the "probability of capturing the most sensitive [bird] species is roughly 0.3%" when considering that only 2 avian species are required to be tested and there are 650 avian species in the US. Additionally, results among standard test species (e.g. the bobwhite and mallard) indicate that it's difficult to make generalizations regarding pesticide sensitivity as responses are often chemical specific and can vary by orders of magnitude even in closely related species. Luttik and Aldenberg (1997) recommend extrapolation factors for birds and mammals based on species sensitivity distributions. Where only 2 birds are tested they recommend an extrapolation factor of 0.051 to provide a reasonably conservative estimate of toxicity to other birds (i.e. you multiply the LD50 by 0.051). Reference: Luttik R. and T. Aldenberg. 1997. Extrapolation factors for small samples for pesticide toxicity data: specific

focus on LD50 values for birds and mammals. *Env. Toxicol. Chem.* 16: 1785-1788.

There is some evidence to suggest that amphibians may be more sensitive to pesticides than the vertebrate species that are currently required (e.g. reference Davidson, Shaffer, and Jennings. 2001. Declines of the California red-legged frog: Climate, UB-B, habitat, and pesticide hypothesis. *Ecological Applications*, 11(2): 464-479). However, knowledge about the sensitivity of amphibians compared to fish or birds is limited given there are no test requirements for amphibian species and that information that exists for non-regulatory studies is often not directly comparable. There are instances when extrapolations about contaminants have been made based on physiological or life history characteristics of organisms that don't break down across taxonomic lines (e.g. fish-eating birds have less monooxygenase activity for xenobiotic metabolism, birds with diets high in protein or calcium are less susceptible to lead poisoning, etc.). This kind of data may be few and far between, but this stresses the need to look for any specific data that may exist, including compounds with similar modes of action and known chemistries, when considering an appropriate safety factor. Consequently, given the uncertainty that exists when extrapolating between classes, the FWS believes it makes sense to suggest an even more conservative approach when extrapolating between classes. In addition, implementing extrapolation factors would provide registrants an incentive to address the uncertainty.